

# CIGARETTE SMOKING AND CARDIAC OUTPUT

BY

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Although the hæmodynamic responses to cigarette smoking have been extensively studied, considerable controversy still exists as to the presence or degree of deleterious effects on the circulatory system (Roth and Shick, 1958). There is, however, general agreement that nicotine is the pharmacologically active substance in tobacco smoke (Comroe, 1960; Haag, 1940; Roth, 1960). From 1 to 4 mg. of nicotine is absorbed into the blood stream during the smoking of one cigarette when the smoke is inhaled (Pierce, 1941). Excitation of the adrenal medulla and peripheral sympathetic ganglia occurs with a resultant tachycardia and a rise of the circulating epinephrine level followed by stimulation of the supra-optic nuclei with the subsequent release of posterior pituitary hormone causing mild pressor effects (Burn, 1960).

It has been postulated that either a constriction of coronary arteries or an increase in the work load of the heart beyond the ability of the coronary vessels to supply the myocardium with essential metabolic demands occurs as a result of cigarette smoking. "Tobacco angina" has been reported by Moschowitz (1928), electrocardiographic changes by Russek, Zohman, and Dorset (1955), and changes in the ballistocardiogram by Thomas, Bateman, and Lindberg (1956). Bellet *et al.* (1962), using coronary sinus catheterization in dogs, reported an increase in the cardiac output and the coronary artery blood flow after intravenous nicotine, which was less in those animals in which coronary artery narrowing had been artificially created. This is in agreement with the work of Barger *et al.* (1957) who found an increased coronary blood flow and decreased coronary vascular resistance in normal men during cigarette smoking. It is possible that the acute effects of smoking may aggravate heart disease but there is as yet no basis on which to incriminate smoking in the pathogenesis of coronary or other types of heart disease.

Bruce and Shillingford (1962) have recently developed a dye dilution technique for recording serial changes in cardiac output: we have used this technique to study the effects of cigarette smoking and intravenous nicotine on the cardiac output to determine the changes, if any, that occur.

## SUBJECTS AND METHODS

Five normal volunteers and 15 hospital patients were studied. They ranged in age from 19 to 66 years. All had smoked at least 15 cigarettes a day for five years or more. They were asked to refrain from smoking for at least three hours before the test which was explained in detail to each one. The patient lay on a couch in a quiet cardiac catheterization room. Standard electrocardiogram leads were connected and pulse and blood pressure were recorded.

A length of P.E. 50 polythene tubing was passed through a transfusion needle inserted into a median cubital or basilic vein and advanced until the distal tip was in the axillary vein. The needle was then removed and a three-way stopcock attached to the other end of the plastic tubing. An intravenous drip of normal saline was attached to one opening of the three-way stopcock for flushing the tubing. Injections of dye were made through the remaining opening of the stopcock: 2 ml. of 2 per cent Coomassie blue dye (40 mg.)

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were used for each determination of the cardiac output. Trafuril (Ciba) was applied to the pinna of the ear and a Cambridge earpiece cuvette was attached to the ear with adhesive tape and connected to a Cambridge dye dilution recorder.

The subject was then allowed to lie quietly and approach a basal state, at which time three dye curves were recorded at five-minute intervals. If it appeared that the curves were varying in area, and thus the cardiac output altering, further curves were made until a stable state was reached. In order to eliminate factors such as the influence of respiration, the following procedures were carried out. The patient was given an unlit cigarette which he "sham" smoked. After measurements of cardiac output had been made the cigarette was lit and the patient smoked it, but without inhaling the smoke. Further measurements were made and then a second cigarette was provided which was lit, and the subject smoked and inhaled. At least five minutes separated each procedure. Further curves were obtained at 10-minute intervals after the cessation of smoking. Standard brands of commercially available cigarettes were used. One study was made in a patient who smoked a pipe as well as cigarettes. In one patient a femoral artery puncture was also done using a Seldinger catheter and arterial photo-electric cuvette as well as the earpiece cuvette to compare the two techniques and thereby determine if the earpiece was influenced at all by vascular changes in the ear possibly caused by nicotine. Two further patients were given nicotine acid tartrate intravenously to determine the effect of that compound on the cardiac output, pulse and blood pressure: 0.6 mg. of the active base were injected through the intravenous cannula, followed by dye curve estimations of the cardiac output.

The area of the curves obtained was calculated and the initial curves obtained during the basal state were averaged to make a control cardiac output of 100 per cent. Subsequent curves were calculated as an increase or decrease of the control figures. The stroke volume was calculated as a percentage from the cardiac output and the pulse rate.

#### RESULTS

Fig. 1 illustrates the effect of smoking two cigarettes within ten minutes of each other. During the first cigarette the cardiac output rose to 156 per cent and the pulse rate increased from 72 to 95 a minute. The stroke volume increased to 115 per cent. During the second cigarette the cardiac

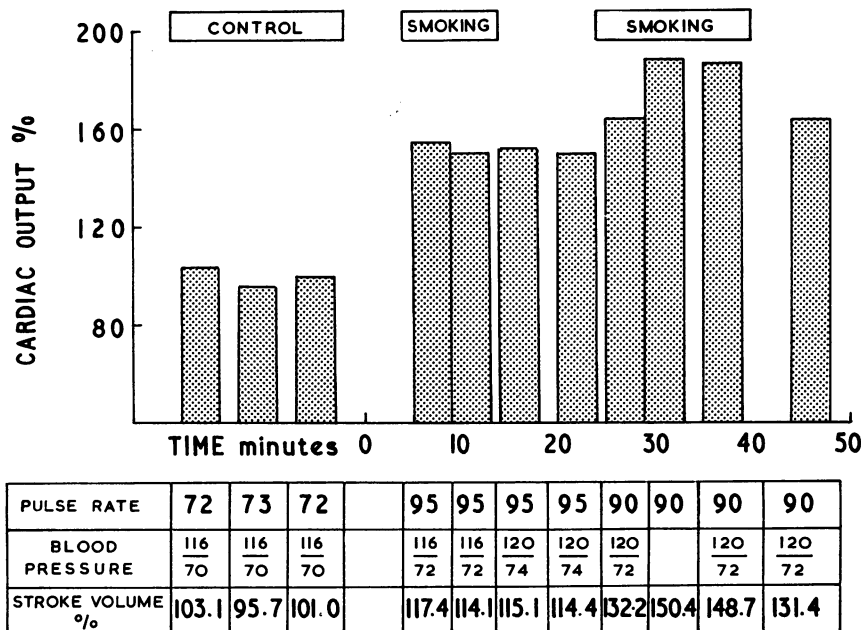


FIG. 1.—The effect of smoking two cigarettes within 10 minutes of each other.

output increased further to 188 per cent and the stroke volume rose to 150 per cent. The pulse rate was 90 a minute.

The effect of "sham" smoking can be seen in Fig. 2. During this procedure, the cardiac output, pulse rate, and stroke volume remained at the same values as during the control period. However, when the smoke was inhaled from a lit cigarette the cardiac output increased immediately to 120 per cent and after the cigarette was half consumed to 152 per cent. The pulse rate, systolic blood pressure, and the pulse pressure also increased, and the stroke volume rose to 113 and 139

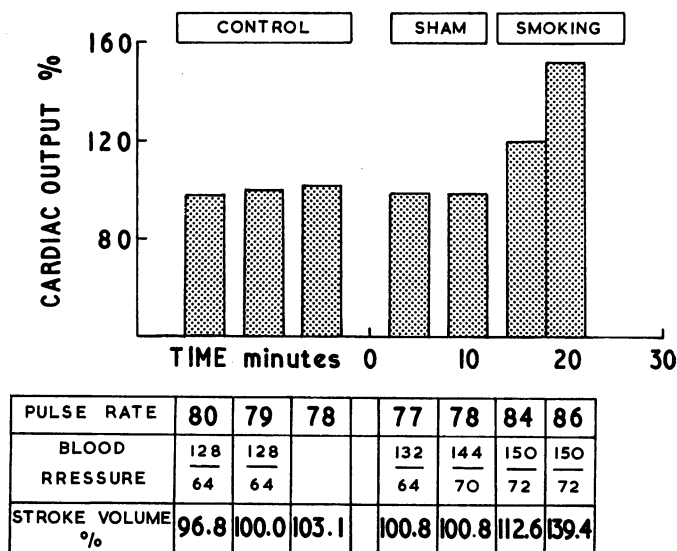


FIG. 2.—The effect of "sham" smoking an unlit cigarette followed by smoking a lit cigarette.

per cent. Fig. 3 illustrates the changes that occur in the cardiac output during inhalation of cigarette smoke as opposed to the effects of "sham" smoking and smoking but not inhaling. The cardiac output, pulse rate, blood pressure, and stroke volume remained at control values until the cigarette was lit and the smoke inhaled. At this time the cardiac output rose to 196 and 170 per cent, the systolic pressure to 122 mm. Hg and the stroke volume to 175 and 144 per cent. The cardiac output and stroke volume were beginning to return toward control values 11 minutes after ceasing to inhale the smoke.

The effect of a few inhalations of tobacco smoke are seen in Fig. 4. The cardiac output, pulse rate, blood pressure, and stroke volume remained constant during the control period, sham smoking, and when the cigarette was smoked but the smoke not inhaled; but when there were three or four inhalations of smoke, the cardiac output increased to 135 per cent. This was accompanied by an increase in the pulse rate from 87 to 94 a minute and a rise in stroke volume to 124 per cent. When the balance of the cigarette was smoked but without inhalation of the smoke, the variables returned to control values.

Smoking a pipe caused an increase in the cardiac output of 138 per cent while the stroke volume rose to 129 per cent (Fig. 5). Smoking a cigarette before the pipe caused an increase of 115 and 130 per cent in the cardiac output. The intravenous injection of nicotine acid tartrate in a relatively small dose of 0.6 mg. of the active base caused an increase in the cardiac output of 144 per cent and in the stroke volume of 125 per cent (Fig. 6). This was accompanied by an increase in the

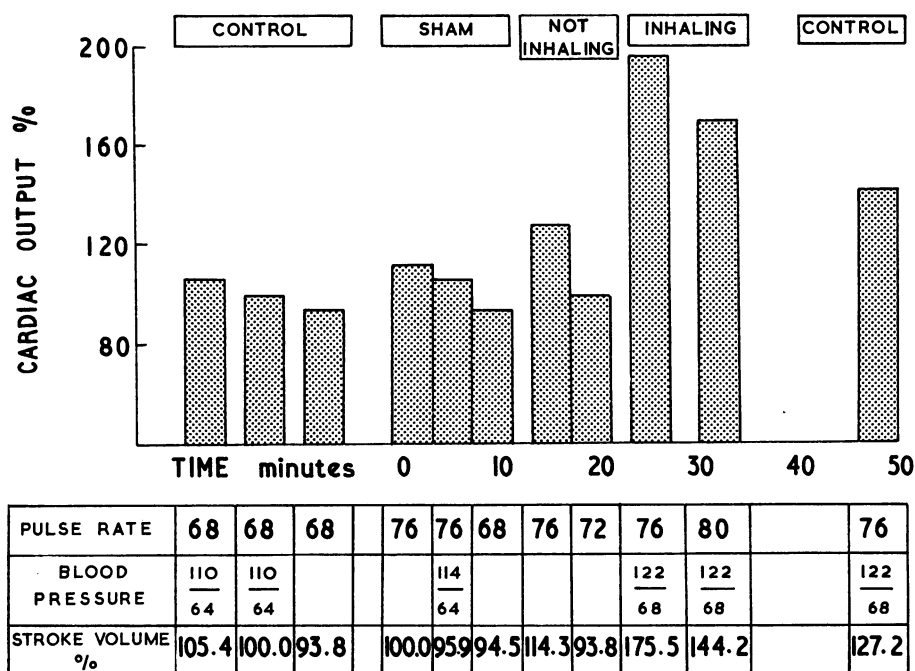


FIG. 3.—The effect of not inhaling, followed by inhaling, cigarette smoke.

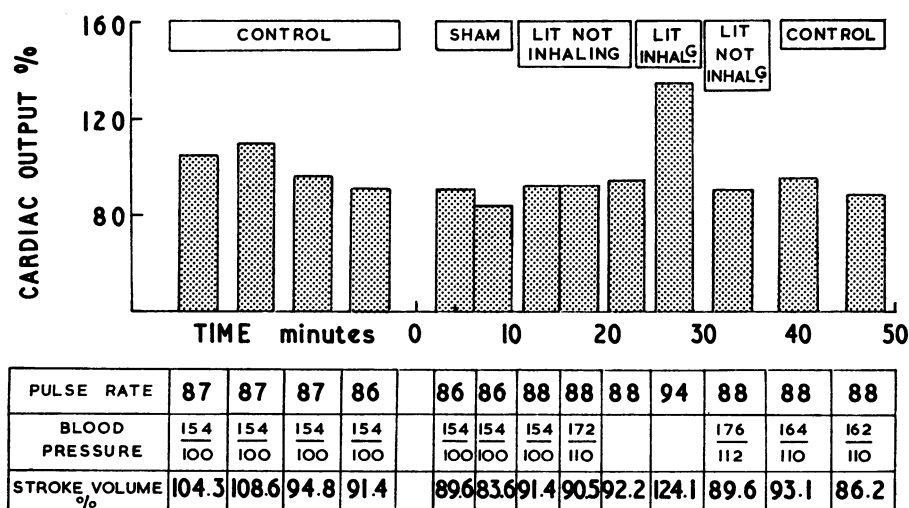


FIG. 4.—Inhalation alone affects cardiac output in this case.

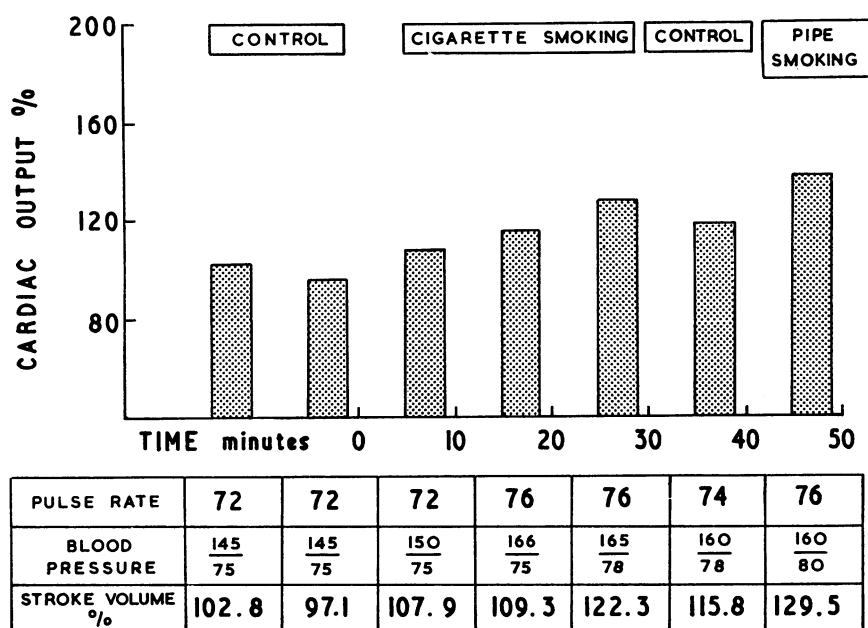


FIG. 5.—Pipe smoking shows a similar effect to smoking a cigarette.

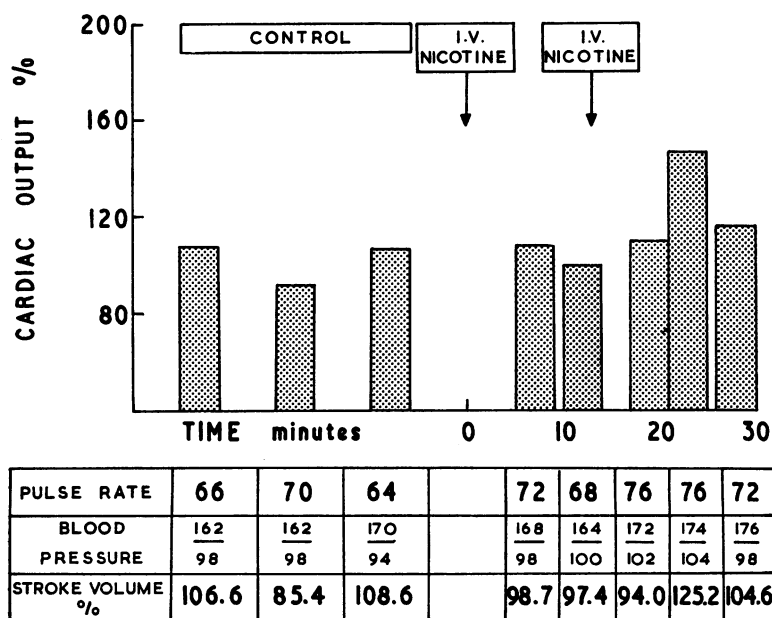


FIG. 6.—The effect of intravenous nicotine on the circulation.

pulse rate from 70 and 64 to 76 a minute and a rise in the blood pressure from 162/98 to 174/104 mm. Hg.

The patient in whom the cardiac output was measured with a Seldinger needle and arterial cuvette as well as the earpiece cuvette showed that the estimations of relative cardiac outputs by these two systems paralleled each other very closely and reflected the same changes. Therefore, it can be assumed that nicotine did not cause a vasoconstriction of the vessels of the ear. Such changes may have been counteracted by the application to the ear of trafuril which caused maximum vasodilatation.

As a further check on the accuracy of the earpiece cuvette, two subjects were each given 20 mg. of Evans Blue dye, and when the tail factor of the dye curve had become stable cigarettes were smoked. If cigarette smoking had caused vasoconstriction of the ear, a fluctuation of the tail factor would have occurred. However, no changes occurred during smoking with inhaling or during sham smoking. This helps to substantiate the validity of the earpiece cuvette technique.

No arrhythmias were recorded on the electrocardiogram in any of the subjects studied, nor was angina provoked.

#### DISCUSSION

These results illustrate the effect of cigarette smoking on the cardiac output. "Sham" smoking or smoking without inhaling does not cause a change, while smoking and inhaling does cause a considerable increase in the cardiac output and stroke volume. Approximately 90 per cent of the nicotine in inhaled smoke is absorbed compared to 25 to 50 per cent of that in smoke not inhaled beyond the pharynx (Goodman and Gilman, 1955). Our results agree with this fact, as there was a much greater increase in the cardiac output when smoke was inhaled than when it was not. The injection of intravenous nicotine also caused an increase in the cardiac output and the stroke volume.

Burn and Rand (1958) showed that intravenous nicotine given to rabbits caused tachycardia by the release of adrenaline and noradrenaline, most probably from chromaffin stores within the atria or as a result of stimulation of atrial post-ganglionic adrenergic fibres. Burn (1960) also suggested that adrenaline or noradrenaline was released from chromaffin tissue in or near vessel walls. The release of noradrenaline may precipitate those arrhythmias aggravated by this substance. Boyle and her colleagues (1947) found an increased heart rate, blood pressure, and cardiac output using the ballistocardiogram after intravenous injection of nicotine. They found a wide variation of response in the individuals studied and found no correlation between smokers and non-smokers or between control patients and those with cardiovascular disease. This work is also in agreement with that of Thomas *et al.* (1956). Henderson (1953), however, noted a greater degree of deterioration in the ballistocardiogram of smokers who had evidence of coronary artery disease than those who did not. He postulated that the observed changes were due to coronary vasoconstriction caused by nicotine.

Bellet *et al.* (1962) measured various circulatory parameters in normal dogs, dogs with coronary artery ligation, and dogs with coronary insufficiency produced by the application of casein rings around the coronary vessels. They found an increase in coronary blood flow and cardiac output following intravenous nicotine, which was less in those animals with coronary artery ligation or coronary insufficiency. They conclude that the increased coronary blood flow during nicotine administration meets the increased myocardial oxygen demand but that this demand is not met sufficiently in animals with a compromised blood flow.

Our studies show an increase in the cardiac output ranging up to 200 per cent over control values during the *inhalation* of tobacco smoke, whether from cigarettes or a pipe, and following intravenous nicotine. Associated with the increased cardiac output is a sinus tachycardia, an increase in the systolic blood pressure, a widening of the pulse pressure, and an increase in the stroke volume. These changes were not seen during "sham" smoking nor when the smoke was not inhaled. The cardiac output begins to return to control values in 10–15 minutes after smoking is stopped.

These studies of the cardiac output during smoking are the first to be reported using a serial

dye dilution technique. The changes in pulse rate and blood pressure that occur during smoking are in agreement with those reported by other workers. The mechanism of an increased cardiac output occurring as a result of the inhalation of cigarette smoke or following the intravenous injection of nicotine is due to the combined effects of an increase in the pulse rate and the stroke volume. Both these variables increased in all patients studied.

#### SUMMARY

The cardiac output during smoking was measured with the dye dilution technique. "Sham" smoking an unlit cigarette or smoking without inhaling caused only slight changes in the cardiac output, while smoking with inhaling caused a large increase in the cardiac output and stroke volume. Intravenous nicotine caused changes in the cardiac output similar to those seen when inhaling smoke. Associated with the increased cardiac output were sinus tachycardia, widening of the pulse pressure due to an increased systolic blood pressure, and an increase in the stroke volume.

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